patients aged < 60 years. Patients aged ≥ 60 years showed improved WOMAC Total score for continuous vs intermittent treatment, but statistical significance was not attained. These data may be useful for health care providers in considering the treatment of OA patients.

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SERUM URIC ACID AS A PREDISPOSING FACTOR OF CLINICO-RADIOLOGICAL SEVERITY OF OSTEOARTHRITIS KNEE

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Purpose: Osteoarthritis (OA) is the most common arthritis worldwide. The association with age, obesity, gender and metabolic factors has been studied widely. Evidence suggests that hyperuricemia is significantly associated with OA of multiple joints. The high level of uric acid involved in cartilage degeneration may modulate radiological features of knee OA. Some study reported that uric acid is associated with generalized OA and other reported that it is a danger signal of increasing risk for OA through inflammasome activation and concluded that synovial uric acid is a marker of knee OA severity. Both OA and hyperuricemia are common in India. This study aimed to investigate the association of serum uric acid with clinico-radiological feature of knee OA in Indian population.
Methods: 180 patients of OA knee diagnosed according to American College of Rheumatology (ACR) guidelines as cases and equal number of controls were enrolled. Clinical OA outcome: pain, stiffness and functional disability were recorded by knee-specific WOMAC index and knee pain was also measured by 10 point VAS. Radiological grading was done by KL grades. In addition, four individual radiological features (IRF)- joint space width, osteophyte, subchondral sclerosis and tibio femoral alignment were also recorded separately. Demographic were recorded by self report. Serum uric acid levels were measured by enzymatic method using Uricase - Peroxidase and analyzed for the interlinking associations.
Results: OA knee cases had significant higher BMI than controls in overall and in both the genders separately. In females, serum uric acid levels were significantly higher in cases in comparison to controls but such association was not observed in males and in overall subjects. Other biochemical variable like random blood sugar and total proteins were not significantly different between cases and controls in any category.
On analyzing serum uric acid level with clinical features, pain (VAS and WOMAC) was significantly associated (p=0.02 and p=0.03) with elevated serum uric acid levels in females; VAS pain alone in overall study population (p=0.024) but not in males. While studying the radiological features, an increase severity of disease (increasing KL grades) was observed with increase in serum uric acid levels (KL grade 4 was 5.26 ± 1.1, KL grade 3 was 4.32 ± 0 .95 and KL grade 2 was 3.63 ± 0.95) in overall subjects and in both the genders separately. No significant association was observed for individual radiological features (IRF).
Conclusion: Radiological severity (KL grade) and knee pain was found to be significantly associated with serum uric acid levels in overall subjects and in females in OA knee.

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PLASMA ADIPOKINES AS MEDIATORS IN EARLY KNEE OSTEOARTHRITIS: DATA FROM COHORT HIP AND COHORT KNEE (CHECK)

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Purpose: Associations of body mass index (BMI) with hand osteoarthritis (OA) have suggested that humoral obesity-related factors may be involved in the pathogenesis of OA. Systemic adipokine levels depend on BMI (amount of fat), gender (different fat distribution between genders), and to a lesser extent age. The purpose of the current study was to determine whether plasma adipokines could be identified as potential mediators of associations of BMI and other demographic variables with radiographic knee parameters in CHECK (Cohort Hip and Cohort Knee), a cohort of (very) early-stage symptomatic knee and/or hip osteoarthritis (OA).
Methods: Plasma (p-) leptin, adiponectin, and resistin levels were determined by enzyme-linked immunosorbent assay. Joint space width (JSW; minimum, mean medial, and mean lateral), osteophyte (OP) area, and subchondral bone density (BD) were quantified in detail on posteroanterior knee radiographs using Knee Image Digital Analysis (KIDA). Mediation analysis was performed to determine whether indirect associations through adipokines could explain (part of the) associations of BMI and other demographic variables with radiographic knee parameters.
Results: Adipokine and radiographic data were complete for approximately 430 CHECK subjects with knee pain. pLeptin was identified as potential mediator of associations of BMI and female gender with JSW. Likewise, pResistin was a potential mediator of an association of BMI with JSW. None of the adipokines could be identified as potential mediators between demographic variables and OP area. pAdiponectin appeared to be a potential mediator of associations of BMI and female gender with subchondral BD. Although statistically significant, associations of demographic variables and adipokines with radiographic knee parameters were weak and adipokines could explain only part of the associations between demographic variables and knee parameters.
Conclusions: Systemic adipokines might be mediators of associations of BMI and gender with JSW and subchondral BD. As such, although their role might be limited, they may play a role in the etiology of (knee) OA.

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THE ASSOCIATION BETWEEN KNEE FUNCTION AND RADIOGRAPHIC OSTEOARTHRITIS IN A POPULATION BASED COHORT - THE MUSCULOSKELETAL ULLENSAKER STUDY

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Purpose: The objective of this study was to investigate the association between radiographic knee osteoarthritis and knee function evaluated by both self-reported questionnaires and performance based tests.
Methods: The Musculoskeletal Ullensaker study (MUST) is an ongoing population-based study of musculoskeletal disorders performed in Ullensaker municipality representing the Norwegian population. Invitation letters were sent to all the inhabitants between 40 and 79 years (n=12000), and those who self-reported either hand, knee, or hip osteoarthritis, verified by their general practitioner, were invited to a clinical examination including functional, clinical, and radiographic measures of the three joints. Standing radiographs using SynaFlexer™ frame for standardized positioning were taken of all the invited participants and scored with the Kellgren and Lawrence atlas (grade 0-4). Osteoarthritis was defined as KL ≥ grade 2. Knee injury and Osteoarthritis Outcome Score (KOOS) was used for measuring pain, symptoms, and activities of daily living (ADL), function in sport and recreation (sport/rec), and knee-related quality of life (QOL). The 30-second Chair Stand test and 6 min-walk test were included to measure performance based function. Multivariate regression analyses with each KOOS subscale and the performance based tests as dependent variable were associated with radiographic osteoarthritis in one knee, adjusted for gender, age, and body mass index (BMI).
Results: Three hundred and twenty three patients were examined between 2010 and 2012 (31% males and 69% females). The mean age was 63.5±8.8 years. Knee osteoarthritis was found in 8.7% for the right knee (n=28), in 6.8 % for the left knee (n=22), and 34 patients (10.5%) had osteoarthritis in both knee joints. Two hundred and twenty seven patients (70%) had no radiographic knee osteoarthritis. Significant associations were found between radiographic osteoarthritis in one knee and the following KOOS subscales: pain (Beta±SE: -13.7±3.7, p<0.000), other symptoms (-13.1±3.1, p<0.000), ADL (-9.4±3.5, p<0.000), sport/rec (-22.7±5.7, p<0.000) and QOL (-21.4±4.6, p<0.000) compared to those without osteoarthritis. No significant associations were found between the 30-second Chair Stand test and 6 min walk test and radiographic osteoarthritis, respectively.
Conclusion: Radiographic knee osteoarthritis was highly significantly associated with poorer self-reported knee function compared to those without radiographic knee osteoarthritis; clinical significant differences were disclosed for all KOOS subscales ranging from 9 to 22 points. However, there was no significant association between radiographic knee osteoarthritis and performance based function.

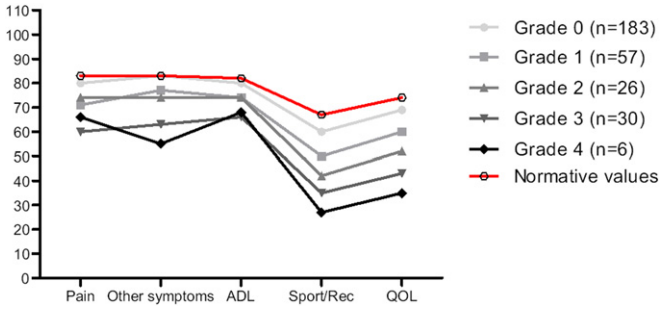

Figure 1. Presentation of the mean values of the KOOS subscales for different grades of radiographic changes in the right knee joint (n=302). Normative values are age matched values from Paradowski et al. 2006.

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IMPACT OF PREDICTABLE VERSUS UNPREDICTABLE INTERMITTENT PAIN ON SOCIAL ROLE PARTICIPATION IN SUBJECTS WITH KNEE OSTEOARTHRITIS

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Purpose: Focus group discussions in individuals with hip/knee osteoarthritis (OA) identified two types of OA pain - a constant background pain and a less frequent, but more intense and often unpredictable, intermittent pain - with the latter having the greatest impact on social role participation. These findings led to the creation of the OARSI-OMERACT measure of Intermittent and Constant OA Pain (ICOAP). The current study sought to validate focus group findings with respect to the influence of OA pain predictability on participation restrictions.
Methods: In an established community cohort aged 50+ years with hip/knee OA, we assessed demographic characteristics, OA pain (ICOAP Knee) and disability (KOOS-PS), and participation restrictions. ICOAP is comprised of two subscales: a 5-item scale assesses constant pain and a 6-item scale assesses intermittent pain, or 'pain that comes and goes'. Subscale scores are created by summing item scores and transforming to 0-100; higher scores indicate greater pain. Those with intermittent pain were asked to report the frequency with which the pain occurs 'without warning' (i.e., unpredictably) and 'after a trigger' (i.e., predictably), from 0 (never) to 4 (very often). To assess social role participation, participants were asked the degree to which they had given up or limited time spent in important roles due to their hip/knee arthritis, from 1, not at all, to 5, a great deal. Logistic regression was used to examine the effect of the frequent unpredictable and frequent predictable intermittent knee pain (often/very often - yes/no) on participation restrictions (roles restricted quite a bit/a great deal - yes/no), controlling for age, gender, and OA severity (ICOAP subscale scores; KOOS-PS score). Specifically, we assessed for interactions between ICOAP intermittent scores and each of frequent unpredictable and predictable knee pain on social role restrictions.
Results: 265 cohort participants with complete data were included in our analyses. Their mean age was 65 years (SD 10) and 75% were female. 69.6% reported intermittent knee pain only, 22.5% constant knee pain only, and 7.9% both pain types. Median (IQR) ICOAP intermittent and constant scores were 37.5 (20.8-45.8) and 0 (0), respectively. Of the 186 subjects who reported intermittent pain, 14.6% reported frequent unpredictable pain and 10.9% reported frequent predictable pain. 40% and 36.6% had limited time spent in 'important roles' 'somewhat' or 'quite a bit'. Controlling for age, sex, ICOAP subscale and KOOS-PS scores, we found a significant interaction between ICOAP intermittent pain severity and frequency of unpredictable pain on participation restrictions ($p=0.03$), such that for individuals with similar levels of intermittent pain severity, the impact on social role participation was greater for those with more frequent versus less frequent unpredictable intermittent pain. No interaction was found between intermittent pain severity and frequent predictable pain.
Conclusion: Our results confirm findings from qualitative research that, controlling for other factors, social role restrictions are greatest among those with intermittent knee pain that frequently occurs warning influences. Further studies in larger cohorts, and with greater variability in pain types, is warranted to confirm our findings and, if confirmed, to elucidate potential explanations.

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EFFICACY AND TOLERABILITY OF CELECOXIB AND NAPROXEN VS PLACEBO IN HISPANIC PATIENTS WITH KNEE OSTEOARTHRITIS

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Purpose: The primary objective of this study was to determine if celecoxib 200 mg once daily (qd) was as effective as naproxen 500 mg twice daily (bid) in the treatment of osteoarthritis (OA) of the knee in Hispanic patients.
Methods: Hispanic patients aged $\geq$ 45 years with diagnosed knee OA in a flare state and with a functional capacity classification of I to III were randomized in a 2:2:1 manner to receive celecoxib 200 mg qd, naproxen 500 mg bid, or placebo for 6 weeks. The primary efficacy variable was the change in the Patient's Assessment of Arthritis Pain at 6 weeks compared with baseline. Secondary efficacy variables were change in Patient's and Physician's Global Assessments of Arthritis from baseline to Week 6/early termination, change in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores from baseline to Week 6/early termination, change in American Pain Society pain scores, score on Pain Satisfaction Scale, Patient Health Questionnaire (PHQ-9) responses, and measurement of upper GI (UGI) tolerability.
Results: 318 subjects were randomized; 239 completed the trial (96 celecoxib, 96 naproxen, 47 placebo) and formed the primary analysis population. Celecoxib was observed to be as effective as naproxen in reducing OA pain (least squares mean change from baseline -39.7, standard error [SE] 2.7 for celecoxib, -36.9, SE 2.6 for naproxen; the lower bound of the 2-sided 95% confidence interval for the treatment difference [naproxen-celecoxib] was above -10 mm). Similar efficacy was seen for celecoxib and naproxen in secondary outcomes. No statistically significant differences between celecoxib and naproxen groups were seen on the Patient's or Physician's Global Assessments of Arthritis, WOMAC Index scores, UGI, Pain Satisfaction Scale score, and PHQ-9. The incidence of adverse events (AE) and treatment-related AEs was similar among treatment groups. 13 subjects withdrew from the study due to AEs (3 celecoxib, 9 naproxen, 1 placebo); 10 discontinued due to treatment-related AEs (2 celecoxib, 7 naproxen, 1 placebo). UGI events (moderate or severe nausea, abdominal pain, and/or dyspepsia) were reported by 3 celecoxib, 4 naproxen, and 1 placebo subject. One subject in the naproxen group had a GI hemorrhage; this was considered a treatment-related AE and resulted in withdrawal from the study.
Conclusions: Celecoxib 200 mg qd was as effective as naproxen 500 mg bid in the treatment of signs and symptoms of knee OA in Hispanic subjects. Celecoxib was shown to be safe and well tolerated in this study population. This information may be of use to physicians treating Hispanic patients with OA.

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RESPONSE TO NONSTEROIDAL ANTI-INFLAMMATORY AGENTS IN ASIAN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE

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Purpose: Celecoxib is an effective treatment for osteoarthritis (OA); however, its efficacy and safety profile has not been extensively studied in different ethnic populations. Differences in therapeutic response to pharmacologic agents have been found in the Asian population, but there are limited data for OA treatments. This study was designed to compare analgesic efficacy, tolerability, and safety of celecoxib, naproxen, and placebo in an Asian American population with OA of the knee.
Methods: Eligible patients in this 6-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study were aged $\geq$ 45 years, of self-reported Asian descent, and with OA of the knee in a flare state and a functional capacity classification of I to III. Patients were randomized to 1 of 3 regimens: celecoxib 200 mg once daily (qd), naproxen 500 mg twice daily (bid), or placebo, in a 2:2:1 ratio. The primary efficacy variable was the change in the Patient's Assessment of Arthritis Pain at Week 6 compared with baseline using a 100 mm visual analog scale (VAS). Secondary efficacy variables included Patient's and Physician's Global Assessment of Arthritis, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Pain Satisfaction Scale, Patient Health Questionnaire (PHQ-9), and American Pain Society (APS) pain scores. Other secondary variables included evaluations of